THE BRITISH JOURNAL
OF
DERMATOLOGY
FEBRUARY 1955

BESNIER'S PRURIGO: AN ECTODERMAL DEFECT.

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In 1892 Besnier presented three patients before the French Dermatological Society to illustrate his thesis that among the multiform dermatoses classified as prurigo, chronic eczema and lichen, there was a group that was distinctive and should be considered apart.

The affection was characterized by intense itching—paroxysmal, often nocturnal and with seasonal exacerbations and remissions. Usually it appeared in infancy or early life. In many cases there were hay fever and visceral manifestations such as asthma and less often gastro-intestinal troubles. The accompanying eczematization, lichenification and sometimes urticaria were in no way specific—the essential was the pruriginous diathesis and the epidermal thickening.

Vidal (1886) had already described his lichen simplex as an entity distinct from eczema, and Brocq and Jacquet (1891) had propounded the view, in elaboration of Vidal's work, that lichenification was a distinct pattern of reaction which could occur alone or in conjunction with other skin reactions, such as the eczematous, and further that it was the reflection of an inborn tendency or predisposition. Vidal, Brocq and others were present at Besnier's demonstration and supported his contention that his cases were illustrative of a distinctive syndrome. It has since received a variety of appellations as the asthma-eczema or asthma-eczema-prurigo syndrome, but throughout this century it has been known as Besnier's prurigo and it is of Besnier's prurigo I propose to speak. I hope this eponymous title will not be replaced by that of atopic eczema, which to me means nothing. In some 8000 cases of eczematous dermatitis I have seen in the past twenty-five years I have never made that

diagnosis. In the first place this affection, as Besnier emphasized, is not essentially an eczema, and in the second place the word atopic means exactly nothing, except perhaps in the mind of Coca (1931). I only hope that the identity of this condition is clearly understood and that we shall not have to subscribe to Sulzberger's ironical remark that the patients under this diagnosis who go to the allergist are quite different from those who go to the psychiatrist, who again are quite different from those who go to the dermatologist—so diverse are interpretations.

Essential Features.

In a fully established case of Besnier's prurigo showing the essential features the whole epidermis is abnormal, thickened, with consequent pallor and carrying a distinctive dirty earthen hue. The pallor may in part be due to the vascular tone consequent upon nervous tension. Portions of the skin may be relatively normal, though head, face and neck, hands and flexures, are particular sites of election. There is often xeroderma. There is commonly, but not always, abnormal pigmentation which may involve the thickened skin only, or the normal skin, or both. It may be diffuse or patchy and there may be areas of leucoderma quite apart from any scars due to scratching. The nails are polished and worn but not usually otherwise dystrophic, nor is the hair except from rubbing. The thickening of the skin with its lack of suppleness and markedly exaggerated lines has all the characters of an animal hide. Whether or not this is entirely due to rubbing and scratching it is difficult to say ; there is much evidence to suggest that it is, but there is clearly, as Besnier, Brocq and others insisted, a great predisposition to react in this fashion to very minimal trauma and it is difficult entirely to remove this feature in a fully established case. It is not merely a reaction secondary to eczema, although secondary eczematization is common. It is a primary reaction of the epidermis and occurs in plaques or sheets, or sometimes in papular form more reminiscent of the old prurigo of Hebra and the reticuloses. Incidentally this, naturally enough, is not at all responsive to corticotropin or cortisone therapy, though any superadded eczema clears at once. I have had patients on cortisone for eighteen months and clear of their eczema and itching but still showing what Besnier called lichenization. The point I am making is that eczema is a mesodermal reaction whereas Besnier's prurigo is ectodermal.

The factor of seasonal variation is usually well marked. We know little about the incidence of Besnier's prurigo in different races or in different climates. We know that with other epidermal disorders, such as ichthyosis and psoriasis, these considerations are significant. Is Besnier's prurigo seen in the Negro or the Eskimo ? My impression from reading the literature is that it is rare. Loewenthal (1936) considers eczema uncommon in the Negro and Ehrström

1951) saw only one case of Besnier's prurigo in his survey of medical ills in Eskimos in Northern Greenland.

The Incidence of Cataract.

If this reaction is then an epidermal or ectodermal reaction we should expect other ectodermal structures equally to show abnormal reactions, and this is the case. The outstanding example is the juvenile cataract—the tendency for the crystalline lens of the eyes to become opaque in early life, usually in adolescence or in the early twenties. A feature is the rapidity with which the whole lens may become involved. This may occur within a few weeks. I have seen it happen in a few days indicating a great instability of structure which must react to some quite minor stimulus, external or internal, or both.

The incidence of juvenile cataract in Besnier's prurigo is given as between 15% and 25% by various authorities. I mentioned some 8000 patients seen by me with eczematous dermatitis : Sixty of these had Besnier's prurigo and 10 of those 60 patients—i.e. about 16%—are known by me to have developed cataract. In private and hospital practice together I have had in all 13 patients with Besnier's disease develop cataract—but it may well be that a number of patients may have developed cataract without my knowledge. Brunsting (1936) reported 15 patients with juvenile cataract in a series of 105 cases at the Mayo Clinic.

It is, however, clearly a serious consideration and I know of nothing that can be done to prevent it. Fortunately, the disease is amenable to surgical treatment. Removal of the cataract and provision of suitable glasses is often quite successful.

The Individual.

We can probably trace ectodermal abnormality beyond this for the ectoderm plays such an important part in the vital characters of the individual—forming the central nervous system and essential features of the endocrine system—that we must expect these subjects to show instabilities in this regard.

They are essentially individualists and are not readily subject to regimentation. Such an affliction as Besnier's prurigo must create in the patient himself and in those around him great stresses and strains and anxieties—but this apart, I believe there is an essential nervous and emotional instability due to the disease itself as it affects the central nervous system. On the endocrine side, in my experience, however, matrimony, pregnancy, and puberty, the climacteric and senility do not often cure or clear or even determine Besnier's prurigo in its major form in the way that is commonly seen with eczema and constitutional reactions. This is not entirely in accord with the reports of some other writers (Loewenthal, 1954).

This inborn abnormality of ectodermal reaction affecting skin, eyes, central nervous system and other organs is perhaps a reaction not limited to ectoderm but involving all structures that in an embryonic sense form the barrier between the individual and the outside world ; that is, ectodermal and hypodermal as opposed to mesodermal structures. It must be regarded as naevoid, a congenital abnormality, probably physiological but possibly structural, though not demonstrable by the ordinary microscope. It may be, however, that studies in biomolecular structure may disclose some actual anatomical abnormality.

Secondary Symptoms.

In practice, of course, the superimposed eczema to which these patients are so regularly subject, the tendency to asthma, hay fever and gastro-intestinal disturbance, demand constant attention from the physician. Sometimes there are specific allergic sensitizations with erythematous and urticarial features which further aggravate the pruritus, causing rubbing and scratching.

But these secondary features, which should not be allowed to obscure the picture, certainly should not persuade us to classify Besnier's prurigo either in the allergic or the psychiatric categories of disease. These fashions in medicine have done something to elucidate the secondary aspects of the problem, but have often confused the primary issue. I do not suggest that they have no place in the management and care of these patients, but it must be appreciated that they are only illuminating certain facets of the problem.

The importance of making a correct diagnosis of Besnier's prurigo lies in the recognition of an ectodermal congenital abnormality which bears seriously upon prognosis and heredity. It is something apart from eczema, which is a mesodermal reaction and immediately responsive to corticotropin. There may be great difficulty in distinguishing the minor or incomplete forms of the disease but I believe that a persistent, intractable flexural lichenification with intense paroxysmal itching starting in infancy or early life, even in the absence of other symptoms or family history, is suggestive and is the minimal requirement for the diagnosis. Some may agree that primary lichenification is often distinguishable from that which is consequent upon eczema.

Onset, Course and Prognosis.

In my figures there is a preponderance of males in the proportion of three to two and a positive family history in 66% of cases. Besnier's prurigo appears to be manifest from infancy in more than 60% (Nexmand, 1948) of cases—80% in my own series—but it may arise later in childhood, in adolescence or even in adult life.

It is difficult to form an opinion as to the probability of a baby with infantile eczema subsequently showing Besnier's prurigo. Figures published suggest between 30% and 40%, but I think that figure is too high; my own figures from about 800 cases of infantile eczema suggest that it is under 5%. The severity of the disease is no guide, though the response to treatment and the appearance of the child may be suggestive, the bonny normal baby being less likely to have the persistent trouble. The family history is often instructive and the early development of flexural lesions is said to be significant. It is, however, rarely until the age of two or three years that one becomes suspicious that the problem is of the Besnier type by which time other symptoms are often manifest.

The diagnosis once established, we recognize that the liability persists through life, though periods of complete freedom are common in the less severe cases. Most of the major cases never clear, although experiencing remissions and exacerbations..

Management and Treatment.

I wish to discuss only a few aspects of the problem of management and treatment which I regard as fundamental. I shall deal briefly or not at all with the treatment of the secondary eczema and asthma.

In the first place, it seems that adjustment to climatic factors is of great importance in achieving the optimum epidermal stability. The same is observed in xeroderma and ichthyosis and in psoriasis. American dermatologists sometimes send their patients globe-trotting until they find the best climate, but this is less easy outside America. A warm dry climate is said to suit many such patients, but Nexmand sent six patients into the upper mountain reaches in Norway and all cleared, only one relapsing after a sojourn of nine months. One of my patients, a parson, always cleared when he did a relief job for a few months in Malta each summer. On the other hand a patient at present in our wards dislikes the summer and looks forward to the onset of winter. Seasonal variation was emphasized by Besnier and is well recognized; most patients in this country prefer the warm weather, but not all, and this seems to depend largely upon sweating. Patients who do not sweat are usually more comfortable in cold weather, and excessive sweating from exercise or emotion will often bring on a paroxysm of itching. It is an important aspect of the pruriginous tendency.

The allergist will attribute improvement consequent upon change of location to the avoidance of adequate allergens and some success has been reported from sojourn in allergen-free rooms and buildings. The psychiatrist (Rogerson, 1939) will see improvement as being due to removal from stress. I believe, however, that it is in fact a climatic and geographical adjustment that is effected, as it is with xeroderma and psoriasis.

Another important environmental factor is the psychological. From the nature of the ill, and its consequences in childhood, patients tend to lack independence and do not easily acquire purposeful occupations. In addition, those responsible are apt to be over-anxious for them and are persistently possessive ; when it is recognized that the parents often have similar temperamental characteristics to those of the child concerned, it is easy to see the difficulties of the situation. It is often an advantage therefore for the patients to be brought up in a completely different—and indifferent—environment but it is usually difficult to get consent for this. And we must not overlook the fact that children with Besnier's prurigo are seen in homes and institutions where there is no parental contact.

A third consideration is that every item of the symptomatology of this syndrome is readily subject to habit formation, and since the patients are commonly children this tendency is probably greater, though adults show much difficulty in controlling themselves.

There is no doubt that corticotropin and cortisone can help considerably in abolishing the troublesome symptoms of itching, eczematization and asthma and will probably be used in the future to control exacerbations or to break bad habits, but they should not be employed until all possible has been done to improve environmental adjustment. Hydrocortisone ointment is of some value, more particularly in dealing with eczematization on softer parts like the eyelids, face and neck, but is of less value where there is much lichenization of the skin or prurigo.

I have not touched upon the judicious use of small doses of sedatives, care being taken not to depress the patient. The use of local applications, especially tar and podophyllin paste, and Grenz or x-rays is sufficiently well recognized. I would condemn the use of antihistamines, both internally and externally. I would, however, repeat what is equally well known, that the sympathy and understanding of the physician and the confidence of the patient are all-important.

Summary.

Besnier's prurigo is an epidermal, ectodermal abnormality which is inborn and is characterized by intense itching, lichenization and general instability.

It is incurable in its major form and is to be regarded as a physiological if not a structural naevoid condition. In milder cases remissions are common.

Juvenile cataract occurs in adolescence or early adult life in about 20% of the subjects of Besnier's prurigo.

Eczema and asthma are secondary but seriously aggravating disorders.

Adjustment to climatic environmental factors is of fundamental importance. There are also fundamental psychiatric factors to be considered.

Corticotropin, cortisone and hydrocortisone ointment have a place in the relief of exacerbations of symptoms and in overcoming habit formation.

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THE ECZEMA-ASTHMA SYNDROME: PSYCHIATRIC CONSIDERATIONS.

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In 1945 I read a short communication on the psychological aspect of this subject when I had been working with Dr. Barber at Guy's Hospital. The most important development that I have noted since that time is the very early onset of the causes of the syndrome. The beginnings of eczema usually occur in the first few months of life and often persist, or disappear only to recur later.

The skin is important in that it is the boundary of the self and the meeting place of the outer and inner worlds. In the first months of life the infant does not differentiate itself and its body from the mother and her body. The skin of its own cheeks and her breast are to it the same, and it is often on the cheek that the eczema starts. Its feelings towards the mother are those to its own body. In all cases of eczema I am sure that we shall find a disturbed mother-child relationship at a very early level of development, that is to say before the ego of the child, its personality, has had time to develop. Anxiety at this early stage is overwhelming and the resulting psychological troubles are not psychoneurotic but psychotic.

In normal development the mother is able to give her child repeatedly and over a sufficiently long and continuous period experiences of good mothering, so that in its psychosomatic structure a knowledge and a belief in a good mother are gradually built up. It has sufficient memories—not necessarily conscious—in its personality to tide it over difficult times. Good mothering includes holding, stroking, bathing and all manner of pleasant skin sensations. The psychological treatment of infants is physical care. The way an infant is fed, held, moved, kept warm, washed, etc., are facets in the development of an inner knowledge of its mother and of the child's own personality.

If, however, a mother is neurotic and in particular if her hate is repressed and unconscious the child feels her hostility in her touch, her voice, her holding, however much she is consciously trying to be a good mother.

I have been seeing at intervals for about 14 months an infant who has developed eczema. The second son of intelligent parents, he has now generalized eczema-prurigo.

The elder brother developed eczema at 3 months which cleared at 6 months and he scratched but little. He was born and lived for some time in the Middle East. The mother was contented and happy and was under the care of a paediatrician who acted

as a parental figure and superintended the baby's feeding and bathing. The child was of a placid nature ; this may have been due partly to inheritance but it was also due to his satisfactory early relationship.

Some time later the mother came to England. She was unhappy, having left her parents and security to start afresh in another country. She had two miscarriages and all through the pregnancy was afraid of losing this baby. The father was very interested in the second son for certain reasons and she was jealous of this. Consciously and materially she was a good mother. Unconsciously she was hostile to the child. I saw the baby at 6 weeks when he had eczema of the face and body. After the interview with me the rash began to clear only to recur a few weeks later—on the day the mother had to attend for a post-natal gynaecological examination and when she feared she was again pregnant. She was full of guilt and feared that if pregnant she would not be able to be the good mother to this child that she was trying so hard to be. By trying so hard she was covering up from herself her hostility to the baby. After a second interview the eczema subsided again, some of her hostility having been made conscious.

At 14 months I saw the mother and baby again. The rash was severe on the arms and legs ; the mother had covered these and the eczema broke out on the face. The child was highly intelligent but made no attempt to move away from the mother and would attempt to walk only if she held his hand and would sit only if he could lean against her. He would hold out his hand for objects but make no attempt to reach them. If the object did not come to the child he would scratch himself. After the mother had had an interview or even a telephone conversation with me the rash would subside. She said it gave her confidence, and her hostility and guilt were to some extent mitigated. However, for two weeks after a later interview the eczema only became worse and I then found that she had received an invitation to visit her parents in the Middle East and take her elder son with her, but felt unable to accept it because she thought she could not leave the baby. She believed that his skin complaint was a punishment to her because her first baby was such a beautiful and admired child. She is expressing her unconscious hostility to this child and using his skin complaint to express her guilt. I have advised her to go away and to leave the baby to the care of a more normal person ; at the same time to leave him in his own environment at home.

What is described as the eczema personality—sensitive, aggressive, insecure, over-dependent, narcissitic—is already present in this baby, but these are really secondary features. He is acting in an abnormal way, his emotional development already affected by the mother's abnormal personality.

The skin is an organ of feeling, both pleasurable and painful, and an infant's feelings are strong and overwhelming. When the mother–child relationship is disturbed the anger for the mother is felt in the child's own skin, which it attacks because it cannot attack the outer mother.

I have tried to express, inadequately I fear, what I have observed clinically, but which has also been stated by Winnicott and Ingram ; by Spitz and Rosenthal, when they state that infantile eczema develops as an attempt to shield the skin from real or anticipated injury, from unpleasant and external stimuli and lack of soothing experiences. The mothers of these infants avoid physical contact with them. As a result of inadequate counterbalancing of unpleasant skin experiences with pleasant ones a hyperalgesic skin state develops which ultimately tends to make them avoid most stimuli from the environment.

I agree with MacAlpine when she says that the psychological basis of the disorder is psychotic not neurotic. By that I do not mean that the patients are insane but that their mental mechanisms are psychotic. One boy of 16 years who was asthmatic had eczema as a baby; he said, " Asthma is my friend, I shall be lonely without my asthma." When the asthma subsided he had to stay for a time in a mental hospital. It may sound as if he was made worse by treatment but it was his road to recovery. It has been my experience not to find patients with eczema in mental hospitals, for once they have become frankly psychotic the eczema is not needed.

I have spoken mainly about children because my experience has been mainly with children. This type of eczema tends to clear at about 2 years of age, probably because at this time the child is beginning to walk and so is more able to leave the mother and find experiences with other people to help in its developing personality. In adults with eczema I think we shall find there has been this disturbed mother-child relationship in early infancy. It is possible that there has been a transient eczema which has passed unnoticed. A baby girl of a mother who had eczema as a child had an eczematous patch on her neck which was almost unnoticed at a few months. At the age of 4 she developed eczema in the flexure of the elbow following the adoption of a child in the family and the return of her father from the war. It quickly cleared, but in times of stress she attacks her skin. This would all pass almost unnoticed except for the fact that her mother, having had severe eczema and being aware of my interest in it, has noted it.

INFANTILE ECZEMA: OBSERVATIONS ON NATURAL HISTORY AND PROGNOSIS

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Early in 1952 we began an attempt to discover what had happened, after an interval of many years, to patients who started life with infantile eczema. The considerable amount of work recorded on the subject of infantile eczema deals largely with aetiology and treatment; we found few facts established concerning natural history, and little to guide the doctor in prognosis.

Consequently, in the standard works these aspects of infantile eczema receive scant mention. Thus, in *Skin Diseases in Children*, MacKee and Cipollaro (1947) comment as follows: "The majority of infants suffering from atopic dermatitis apparently recover by the time they reach the age of three; those who do not, develop the cutaneous manifestations already described" (atopic dermatitis in older children). Similarly, Brain (1949) states: "The mild cases will usually respond to treatment in a few months. Besnier's prurigo is likely to give considerable trouble until puberty and even then to relapse if the skin is exposed to irritation or subject to psychological stress." In neither case do these authorities refer to any accurate data on this aspect.

Slesinger (1948) has reported a series of 60 infants and children, in most of whom eczema disappeared by 15–18 months, though in 16 it persisted into later life; and Purdy (1953) has recently published the interesting report of a postal follow-up of patients who had been treated at hospital for infantile eczema about 15–21 years previously. Of the patients he wrote to, a reply was received from about 60%.

At the outset of our investigation it was decided, first, that a control series was desirable; and, second, that an attempt should be made to obviate inaccuracies inherent in any survey by correspondence. The following report represents the results of our survey. It was confined to a necessarily selected group of cases; any conclusions drawn must be weighted with due regard to this factor, and to the difficulties of any retrospective study.

Material and Controls.

Selection of cases.—The eczema-dermatitis reaction affecting infants and children varies so much in severity and extent that it is difficult to impose a standard for selection. Obviously, the prognosis of infants with a small patch of scaling eczema on the face or behind the knees is unlikely to be the same as that of infants having widespread weeping eczema or large patches at the knee, elbow and wrist flexures. It was therefore arbitrarily decided to review only cases severe enough to have warranted admission to hospital. Even with this criterion it is realized that there must be considerable variation among cases, since many factors not directly connected with the severity of the eczema may determine admission to hospital. Only those patients in whom the condition began before the age of one year were included. No attempt has been made to separate out any particular pattern of infantile eczema, though one case was excluded from the series because an external irritant had played an important part.

From 1930–1940 inclusive there were records of 115 infants or young children with eczema who had been admitted to the United Bristol Hospitals. Thirty-one patients were excluded because either they were untraceable (21 patients), or were traced only as far as an adoption society (4 patients), or replied to a questionary but were not visited (6 patients). During 1952 and 1953 the homes of the remaining 84 were visited by one of us (M. V.). In all but 3 cases (in which the nearest other relative was seen) the mother was interviewed, since obviously she would know more about the patient's past history than would the patient himself. In half the cases the patient also was interviewed. The patient's age at the time of review was 10 14 years in 18 cases ; 15 19 years in 42 cases ; and over 20 years in 18 cases. Six patients had died.

Comparative series.—For comparison, cases with no record of skin disease were chosen from the hospital in-patient records. Each represented a surgical admission, of the same sex as a patient in the eczema series. Each was selected so that the age on admission corresponded to within four months of the age on admission of a patient in the eczema series : with any closer age correlation the numbers available became too small for even a rough comparison. Through paucity of material only 57 cases were available, though there was an even spread over the age groups. These patients' homes were all visited in a similar way to the eczema series ; the mother was interviewed in every case, but only 4 patients were seen.

Because our attempt at a control series had been only partly successful further information, for a rough comparison of morbidity and associated disorders, was obtained from the school records of 120 children chosen because they were of the same sex and age as our children with eczema.

Results.

Death.—Of the 84 patients with infantile eczema 6 had died during infancy (four at 7 or 8 months of age, one at 14 months and one at 29 months). All had some infection : 2 had pneumonia, 2 gastro-enteritis, 1 bronchitis and gastro-enteritis, and one died undiagnosed two days after a sudden rise in temperature.

Persistence of eczema.—The age to which eczema persisted in the remaining 78 patients is illustrated in Fig. 1. In 55% of the cases eczema had persisted

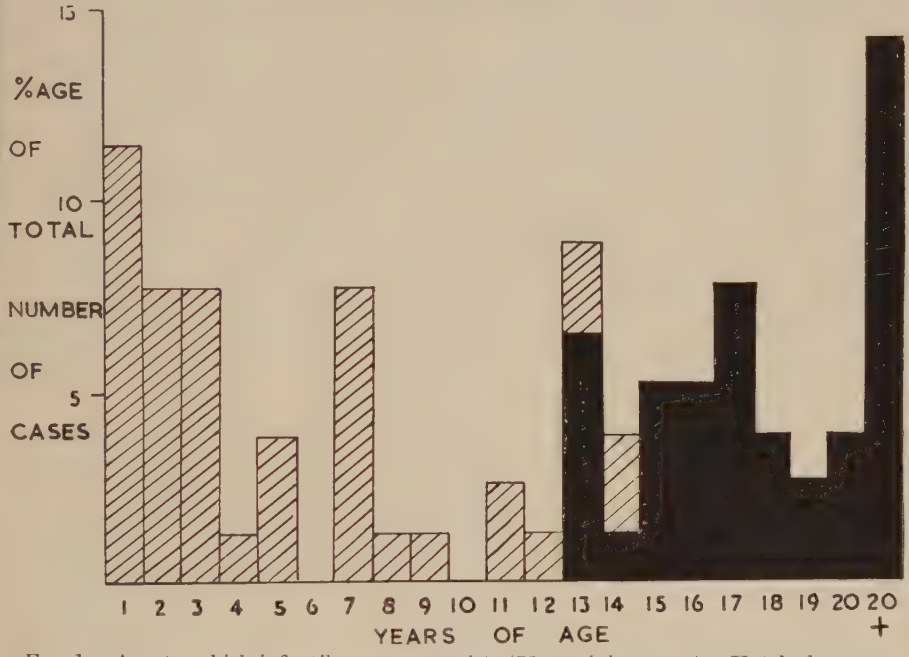

Fig. 1.—Age to which infantile eczema persists (78 surviving cases). Hatched areas show percentage of cases which cleared up at each year of age; black areas show eczema persisting at the age of interview.

up to 13 years of age. As some of the patients were seen while still under 20 years of age it is not possible to give an accurate figure for the persistence rate up to the age of 20 ; it must fall between 18% and 55%, and much nearer the latter figure than the former since the tendency for eczema to clear up in the teens appears to be slight. The period when there is the greatest tendency for eczema to resolve is during the first 3 years, when in 27% of our series the skin became clear.

Associated disorders.—The incidence of associated disorders in the eczema group, compared with the other groups, is summarized in Table I. Seventy-three per cent. of the patients fell into a group comprising asthma, recurrent bronchitis or seasonal rhinorrhoea ; 50% had asthma alone, as compared with much lower figures in the other series of children. Migraine and urticaria

were both much commoner in the eczema series than in the others. It was interesting to find that 22% of the eczema cases had a history of one or more attacks of pneumonia, a figure very much higher than in the comparative series. This tendency was not confined to those cases complicated by asthma for 7 of the 17 patients with pneumonia had not suffered from asthma.

It is apparent from these figures that the severer grades of infantile eczema, which form the group we have considered, carry a considerable morbidity. The eczema persists in a large number of cases and there is a considerable incidence of associated disorders.

TABLE I.—*Incidence of Associated Disorders in Infantile Eczema and in Two Compared Groups.*

History of associated disorders.	Number and percentage affected.		
	Infantile eczema cases.	1st compared group.	2nd compared group.
Total . .	78	57	120
1. Respiratory tract disorders as defined . . .	57 (73%)	2 (4%)	12 (10%)
(*a*) Asthma . .	39 (50%)	1 (2%)	2 (2%)
(*b*) Recurrent bronchitis	13 (17%)	1 (2%)	8 (7%)
(*c*) Seasonal rhinorrhoea	5 (6%)	0	2 (2%)
2. Headache and/or recurrent vomiting . . .	18 (23%)	0	0
(*a*) Migraine . .	3 (4%)	0	0
(*b*) Recurrent headaches	5 (6%)	0	0
(*c*) Recurrent vomiting.	10 (13%)	0	0
3. Pneumonia (one or more attacks) . . .	17 (22%)	0	3 (3%)
4. Urticaria . . .	13 (17%)	0	1 (1%)

SOME FACTORS IN PROGNOSIS.

In an attempt to ascertain factors that might help in arriving at a prognosis in any individual case, the following points from the case histories of the eczema group were established :

1. *Family history of eczema or asthma.*

	Family history.	
	Positive.	Negative.
Average duration of eczema (years) . . .	14·9	8·7

The difference of 6·2 years is statistically significant (S.E. = 2·13).

2. *Position in family.*

	Position in family.		
	Only child.	Eldest.	Youngest.
Average duration of eczema (years) . . .	7·7	11·8	9·85

The difference of 4·1 years between the average duration for the only child and the eldest is suggestive but not statistically significant (S.E. = 2·38).

3. *Number of children in family.*

	Number of children.			
	One.	Two.	Three.	Four or more.
Average duration of eczema (years) . . .	7·7	11·1	12·4	12·4

The difference in average duration for the only child and one with four or more children in the family is 4·7 years. This figure is not statistically significant (S.E. = 2·88).

These figures, though not conclusive, show a tendency for the duration of eczema to be longer *pari passu* with the number of children in the family. When this trend is taken in conjunction with the figures for position in family, it seems to indicate that the duration is less with an only child and greater when there are many children in the family. It should be understood that this point is not statistically proven ; but the figures do not support the opposite, and generally accepted, view that the duration is likely to be longer in an only child.

4. *General state of the skin.*—The skin was assessed as being generally dry (28 patients), greasy (12 patients) or normal (41 patients) by direct observation in those patients interviewed personally or, in the remainder, from the nearest relative's description.

	Condition of skin.		
	Normal.	Dry.	Greasy.
Average duration of eczema (years) .	7·9	14·7	13·3

The differences between dry and normal of 6·8 years (S.E. = 1·58), and between greasy and normal of 5·4 years (S.E. = 2·29), are statistically significant.

If either a dry or greasy state of the skin persists, as a constitutional trait unchanged from infancy, infantile eczema is more likely to persist.

5. *Other factors.*—No significant difference in duration of eczema was found when infants of birthweight less than 7 lb. were compared with infants of birthweight over 8 lb. ; no difference was established on the basis of sex, complexion (dark or fair), breast or artificial feeding. The data were insufficient to permit a comparison, as regards chronicity of eczema, between cases with eczema of early or late onset.

An attempt to assess psychological factors in the patients and the family was made, but it proved so difficult that it was regretfully abandoned.

The facts established, therefore, appear to be that eczema is likely to persist longer when eczema or asthma has occurred in siblings, or when the patient's skin is more greasy or more dry than the normal. On the contrary, it is not more likely to persist in an only child ; and indeed there is a suggestion that the duration is likely to be longer when there are several children in the family. Birthweight, sex, colouring, and type of infant feeding do not seem to influence the tendency to persist.

Discussion.

In his postal follow-up Purdy had replies from 93 patients (60%) who had attended the hospital out-patient department with infantile eczema 15–21 years previously : 15–28% were assessed as having Besnier's prurigo, roughly 30–50% had had asthma, 9–15% had hay fever, and 4–8% migraine. These figures show the heavy rate of persistence and of associated diseases which we also have demonstrated ; but it must be remembered that they apply only to infantile eczema severe enough or persistent enough to warrant attending hospital. As has already been pointed out, our own figures apply to a grade of infantile eczema at least as serious, since it necessitated hospital admission. Obviously there are many degrees of severity of infantile eczema, from the mildest to the most severe ; we believe, though we have no statistical proof, that, as a rough guide, in a series of infants the prognosis is progressively better as the severity of eczema is less. For the common milder grades the prognosis is probably excellent and the occasional transient patch will usually clear without any sequelae.

In our series a surprisingly high mortality rate (7%) appears, and we draw attention to somewhat similar figures in Purdy's series. It must be remembered, however, that in the years 1930–1940, from which our cases were drawn, the infant mortality rates for Bristol varied between 57·5 and 42·3 per 1000. But all our children were seen for the first time after the first month of life, during which period a large proportion of infantile deaths occur ; so that the mortality rates for our children should, in fact, be much lower than the total annual figure. Only one patient died in the two groups of patients which we compared with our eczema series, and his death was due to drowning. The death rate in the eczema series is several times higher than would be expected ; but on analysis the difference is not statistically significant (at the 5% level) when the usual correction for such small numbers is applied. All of our cases who died had secondary infection and most deaths occurred before sulphonamides and antibiotics were available, so that the mortality is almost certainly much lower to-day.

It was interesting to find that 22% of our cases had had one or more attacks of pneumonia. This association of pneumonia and eczema has also been demonstrated recently by Hewitt (1954) in a survey of adult dermatological hospital in-patients made at Bristol. He found that among 208 patients with eczema 11% gave a history of one or more attacks of pneumonia, as contrasted with 42 psoriasis patients of whom only 2% reported having had pneumonia.

Summary.

A series of 84 patients has been followed up by visits to the home 13–22 years after admission to hospital with infantile eczema.

Six died in infancy with some infection. Of the remaining 78 one-quarter cleared up by 3 years of age. Eczema was still present by the age of 13 in 55%. By the age of 20 eczema still persisted in a considerable proportion.

Asthma, recurrent bronchitis or seasonal rhinorrhoea were present in 73% of the patients, as compared with 5–7% of compared groups. Fifty per cent. had asthma alone as compared with 2% in other groups. One or more attacks of pneumonia had occurred in 22% of the patients, but in only 2% of compared groups.

In the assessment of prognosis it appears that the skin disorder is likely to last longer when there is a family history of eczema, or when the skin is more greasy or more dry than the normal. It is not more likely to persist in an only child; birthweight, sex, colouring, and type of infant feeding do not appear to influence the tendency to persist.

Our thanks are due to Prof. A. V. Neale for helpful suggestions and cooperation.

We are indebted to G. Herdan, M.Sc., Ph.D., Ll.D., Lecturer in Statistics, University of Bristol; to Miss E. H. L. Duncan, M.A., B.Sc., Records Officer, Department of Public Health, and to Dr. R. C. Wofinden, M.D., D.P.H., D.P.A., Deputy Medical Officer of Health for Bristol, for advice and help with statistics.

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SKIN REACTIONS IN ATOPIC ECZEMA.

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In the investigation to be described skin tests were performed on a group of children suffering from infantile eczema and Besnier's prurigo in order to determine the incidence and nature of positive reactions. An attempt was then made to discover whether, in this group of children, the results of these tests were of any value in the diagnosis and prognosis, or as an indication for treatment of this skin disorder. The children investigated were all in-patients and most of them were under observation for a long period before and throughout the time during which the various tests were carried out.

There were 112 children suffering from infantile eczema and Besnier's prurigo, and 43 children suffering from other skin diseases were taken as a control group (Table I).

Table I.—*Number of Patients.*

Infantile eczema and Besnier's prurigo	112
Control patients :	
Impetigo contagiosa	16
Psoriasis	9
Papular urticaria	5
Infective eczema	4
Discoid eczema	3
Pompholyx	2
Epidermolysis bullosa	2
Urticaria	1
Summer prurigo	1
Total	43

Tests were carried out with standard skin testing extracts by the scratch method. The individual substances producing positive reactions were determined and the tests were repeated after approximately six months in as many of the children as possible. The results of these tests showed that, while all the control group of patients had negative reactions, 73 (65%) of the eczema patients were positive to one or more test substance. The incidence of positive reactions increased with age so that, while about half of those under four years gave positive reactions, 90% of the children over seven reacted to one or more test substance (Fig. 1). Reactions to egg were most frequent in the children under two and became less frequent in older patients, while the reverse was the case for pollens (Fig. 2). Positive reactions were obtained to all the food substances tested, but to very few of the other test substances—textiles and

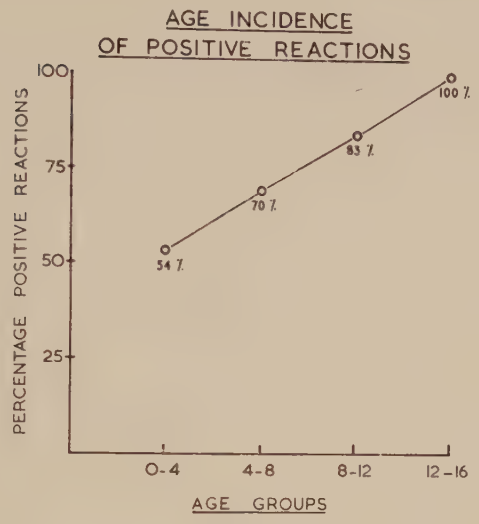

Fig. 1.

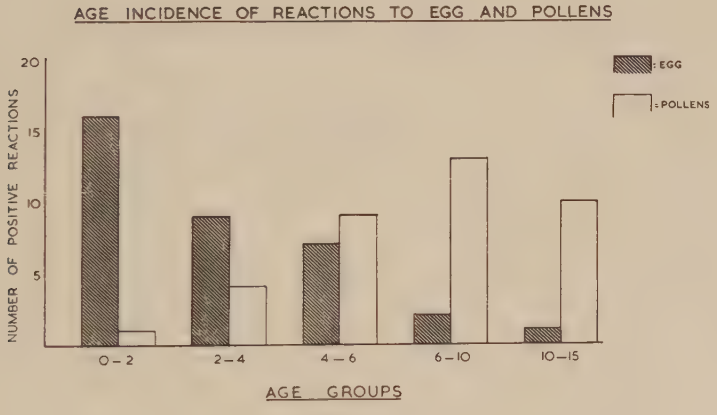

Fig. 2.

inhalants other than pollens. Only two children reacted to milk and they were both between four and six years old (Table II).

Table II.

Age group (years).	Number of patients.	Positive reactors. Total.	Positive reactions. Cereals.	Egg.	Pollens.	Milk.	Vegetables.	Fish.
0–2	33	17	—	16	1	—	2	1
2–4	28	16	2	9	4	—	1	2
4–6	18	16	2	7	9	2	1	1
6–10	21	13	4	2	13	—	2	3
10–15	12	11	5	1	10	—	1	1
Total	112	73	13	35	37	2	7	8

Of the cases of atopic eczema 17% suffered from asthma or had had attacks of asthma before admission to hospital. As attacks of asthma are quite uncommon in these children while they are in hospital, I have included in the total of children suffering from asthma all those who had a history of having had attacks of asthma in the past. It was rather more common in the older children, and all those suffering from asthma gave positive reactions with either pollens or egg, most frequently with pollens (Fig. 3).

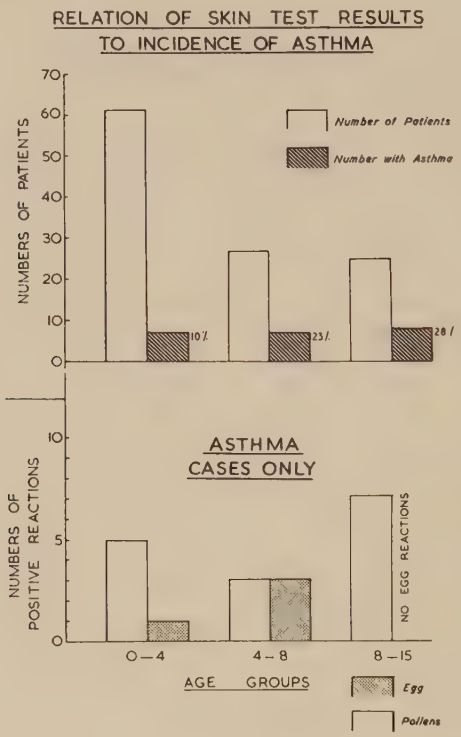

Fig. 3.

In general, these results are similar to those reported by Hill and Sulzberger (1935), who found that foods, particularly egg, gave positive reactions in infants and that inhalants gave positive reactions more frequently in older children and adults. This fact was mentioned by Cranston-Low (1928) in his paper on the eczema-asthma-prurigo complex ; he also discussed the association of asthma with eczema of this type and concluded, from studying the reports of over 200 patients, that the incidence of asthma was about 15%—approximately the same as in the present group of patients.

Tests were repeated in 68 children after six months had elapsed. Identical reactions occurred in 67% of them. A small number changed from positive to negative and *vice versa*, and 19% were still positive to one or more of the

same substances as before but showed different reactions to other groups. In short, the reactions after a lapse of six months were virtually the same in 85% of the children in whom the tests were repeated (Table III).

TABLE III.

Controls : 8 repeated	still Negative.
Atopic eczema : 68 repeated with the following results—	
Negative, still negative	20 (30%)
Positive, still positive	25 (37%)
Positive, previously negative	8 (11%)
Negative, previously positive	2 (3%)
Still positive but to some different groups	13 (19%)

There appeared to be no relation between the incidence of positive reactions and the severity of the skin affection, and indeed many of the most severely affected were negative to all the tests.

As Hill (1951) had suggested that contact sensitivity to wool played a part in the occurrence of relapses of infantile eczema during the winter, patch tests with wool were performed on most of the children under investigation. Only two doubtfully positive reactions were noted in the 81 children with eczema in whom this test was carried out.

A Prausnitz-Küstner test was performed with the serum from children sensitive to egg, cereals, fish and pollens respectively. These were all positive, the antigens being administered to the test subject by mouth in the first three cases and by intracutaneous injection when testing the sensitized site with pollens.

An attempt was made to determine the effect of eliminating egg from the diet of a group of children sensitive only to egg as shown by the scratch test results. Egg was completely eliminated from their diet for three weeks and any clinical change noted. For the next three weeks egg was given as freely as practicable. Eight of the 29 children dieted in this way developed urticarial reactions a few minutes after eating egg, but in only two of these did the state of their eczema become worse. In the other 27 there was no evidence that the presence or absence of egg in their diet had any influence upon their skin disorder (Table IV).

TABLE IV.—*Three Weeks' Diet Containing No Egg followed by Three Weeks' Diet in which Egg was given Freely.*

Number of patients (all positive only to egg)	29
Improved throughout 6 weeks' diet period (Immediate reactions to egg, 3)	11
Remained the same throughout the diet period (Immediate reactions to egg, 2)	11
Became worse on the egg-free diet (Immediate reaction to egg, 1)	5
Improved on egg free diet but became worse on taking egg again (Immediate reactions to egg, 2).	2

Six children who reacted only to pollens were given a course of injections of pollen extracts in an attempt to desensitize them. This was not completed in one child, who developed severe urticarial reactions after each injection but without any worsening of her eczema. The other five children did not appear to be affected by the pollen injections and when they were retested at the end of the course they were found still to be positive to pollens.

The results of skin tests in this group of children show that they may have some diagnostic value. This is indicated by the fact that nearly two-thirds of the eczema patients gave positive reactions while not one of the control group reacted. On the other hand, the results of such tests do not appear to be related in any way to the severity of the skin disorder or to have any prognostic significance. The elimination of egg from the diet of children in whom the skin tests were positive only to egg did not have any effect upon the course of their eczema, nor did the addition of egg. This confirms the widely held view that such sensitivity is only incidental to the atopic constitution and not of any aetiological significance.

Summary.

Positive skin tests occurred in two-thirds of the children with atopic eczema while all the children in the control group were negative to these tests.

Over 80% of the children tested gave virtually the same results six months later.

Reactions to egg were the predominant positive result in the first three years of life; older children were more often positive to pollens.

Asthma occurred in 17% of the children and of these 80% were positive to pollens and 20% to egg.

Elimination of egg from the diet of egg-sensitive children did not influence their eczema although some produced immediate urticarial reactions when given egg.

Skin tests may be of some diagnostic significance but in this group of children were not related to the severity of the skin disorder.

I wish to thank Dr. G. B. Dowling for his kindness in allowing me to investigate these patients who are under his care at the Goldie Leigh Hospital.

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BESNIER'S PRURIGO: OBSERVATIONS ON ABNORMAL CUTANEOUS AND CENTRAL NERVOUS REACTIONS.

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The essential pathogenesis of Besnier's prurigo is unknown and controversy persists as to the relative importance of various precipitating and aggravating factors.

The influence of heredity is indicated by the family histories and by the frequent co-existence of ichthyosis, a disorder of established genetic origin. In a survey recently carried out, ichthyosis was present in 8 of 58 patients suffering from Besnier's prurigo. Nevertheless it is doubtful how much Besnier's prurigo itself is of genetic significance and how much it is due to environmental influences in early life. One of us has recently seen two pairs of identical twins, in each pair of whom only one child showed signs of Besnier's prurigo. Probably both the inheritance and the environment are important contributory factors. The inherited factor appears to be an immunologico-autonomic perversion of defensive over-awareness, and the environmental factors are various infections, emotionally stressful situations, and changes in the physical environment. To quote Hill (1952): "It is as much a definite constitutional disease as is diabetes or epilepsy."

The concept of allergic hypersensitivity is no longer tenable. Specific hypersensitivity can rarely be demonstrated and, as O'Leary (1953) has pointed out, positive skin tests that are sometimes obtained are usually only indicative of general over-activity of the skin.

The two systems, immunological and autonomic, cannot logically be separated. They play interdependent roles in the defensive mechanism of the whole individual. The most significant characteristic of the pruriginous patient is a combination of abnormal immunological responsiveness and autonomic imbalance; the former shown by excessive reactiveness to virus infections and to inoculation with egg-white: the latter by asthma, vaso-motor rhinorrhoea, lability in sweating and a tendency to cutaneous vaso-constriction, as revealed by facial pallor and white dermographism. Pulay (1921) noted vascular hypotension and regarded the itching of Besnier's prurigo as a manifestation of vagotonia; Müller (1930) noted a tendency to hypoglycaemia.

Some writers place great emphasis on a faulty mother-child relationship in Besnier's prurigo ; but all children subjected to " maternal rejection " do not suffer from Besnier's prurigo, suggesting that an individual abnormality of response is most important and " maternal rejection " only one of many emotional, infective and physical noxae that may disturb these patients. McLaughlin *et al.* (1953) have pointed out that " the general pattern of personality defect seen in these patients is similar to that described for a variety of psycho-somatic disorders, namely excessive passivity and clinging dependency, coupled with a crippling inhibition of aggressive and erotic drives."

Seasonal and climatic influences have probably been exaggerated. In a survey of 52 patients with Besnier's prurigo recently carried out, 6 stated that they were worse in the spring, 12 in the summer, 6 in the autumn, and 13 in the winter, while 15 thought that seasonal changes had no influence on the malady.

Eyster *et al.* (1952) state that in atopic but not in normal subjects or in those with other dermatoses, there is swifter cooling in a cool environment, and delayed warming in a warm environment, seeming to indicate a greater constriction of peripheral blood vessels. Vasoconstriction is a normal response to exposure to a cold environment, emotional stress, fear, anger, fatigue or loss of sleep ; but in atopic subjects an exacerbation of the symptoms also results from these stimuli. Eyster also noted an excessive rise of blood pressure in patients with Besnier's prurigo on exposure to cold.

With these data in mind, we decided to study the reactivity of the skin and of the central nervous system in this disease.

The Skin.

Before describing the abnormal reactivity of the skin in Besnier's prurigo, it is well to recall the physiological response of the skin to friction. According to Evans (1952) gentle stroking results in transient flushing followed by the appearance within 15–20 seconds of a white *tache* or mark ; firmer pressure causes a slight flush followed in 15 seconds or so by a much deeper flush in the line of friction, with a white *tache* on both sides of the red flush. These reactions fade in from 3–8 minutes.

In Besnier's prurigo, light or firm stroking at sites affected by the disease is followed in 7–15 seconds by blanching confined to the line of friction. A marginal white *tache* is not visible. The white line slowly fades and disappears after a few minutes but can be reproduced at the same site by further friction. At sites not affected by the disease the normal red line develops on firm stroking, and the white *tache* on either side of it is most conspicuous. In slightly affected areas an intermediate picture may be seen of faint pinkness in the line of stroke and marked pallor alongside.

According to Dale (1950) the tone of the minute blood vessels, which is abolished by histamine, is normally maintained by some agency other than the sympathetic nerves and adrenaline. This substance may be acetylcholine, which is continually synthesised in muscles and blood vessels (Burn, 1950).

A priori, one would expect the white line of Besnier's prurigo also to be independent of central or peripheral nervous connections. Evaluation of its dynamics should nevertheless be helpful towards a fuller understanding of this disease; it was therefore decided to attempt to modify or to obliterate white dermographism (replacing it by a red line), by applying heat and cold, by local intradermal injections of various substances, by local cutaneous anaesthesia and by sympathetic block. Results of these experiments are shown in Table I.

TABLE I.

Purpose.	Substance used.	Method.	Effect on Dermographism.
Effects of cold	Iced water	Applied to surface	None
Effects of heat	Hot water	,, ,,	,,
Cholinesterase antagonist	Eserine 1/10,000	Intradermally	,,
Acetylcholine antagonist	Atropine 1/10,000	,,	,,
Histamine antagonist	Adrenaline 1/10,000	,,	,,
Adrenaline antagonist	Dibenamine 1/10,000	,,	,,
Adrenaline antagonist	Histamine 1/10,000	,,	White dermographism diminished
Antihistamine	Anthisan 1/10,000	,,	None
Acetylcholine analogue	Carbachol 1/10,000	,,	,,
Histamine-releasing agent	Compound 48–80	,,	White dermographism eliminated
Control	Distilled water	,,	None
Local anaesthesia	Xylocaine	Subcutaneously	,,
Sympathetic block	Procaine	Cervical sympathetic	,,

These findings suggest that white dermographism is due, partly or wholly, to non-liberation of histamine at sites of repeated friction, perhaps because the cells have become refractory to this type of stimulus, though not to the injection of compound 48 80. This substance is the most potent histamine-liberator known—one molecule of it liberates 80 molecules of histamine. The concept of a local deficiency of histamine is supported by the findings of Williams (1938) that whereas in normal individuals an injection of histamine produces an increase of skin temperature at the face and neck, in pruriginous persons the rise also occurs at sites affected by the disease, namely on the upper chest and at the bends of the elbows and knees. In the early stages of an attack, before the refractoriness develops, the violent scratching and rubbing must cause considerable liberation of histamine with remote effects

comparable with those caused by an intramuscular injection of histamine. Histamine liberated by scratching may be responsible for asthma and vasomotor rhinorrhoea, and its non-liberation when the lichenification is at its height may explain the apparent alternation of asthma with prurigo described by some patients.

According to Nexmand (1948) prurigo usually appears before the asthma and although asthma sometimes alternates with prurigo, the itching usually becomes worse with the asthma or hay fever.

It can be argued that the deficiency of histamine is brought about by its antagonism by an excess of adrenaline or *nor*adrenaline, but this would be accompanied by general vasoconstriction and hypertension ; and further, the injection of dibenamine, an adrenaline antagonist, was not seen to have any effect in diminishing the intensity of the white line.

It appears, then, that white dermographism is due to an abnormal tonicity inherent in the cutaneous blood vessels and independent of the peripheral nerve supply and of stimuli from the central nervous system, persisting as it does after local anaesthesia and after sympathetic block. It is due to a local imbalance of chemical neuromuscular stimulants in favour of those that cause increased tonicity of unstriped muscle (? acetylcholine). Non-removal of acetylcholine because of a deficiency of cholinesterase is also, theoretically, possible.

The intense itching of Besnier's prurigo may also be due to histamine which, according to Feldberg (1954), is the main physiological stimulus for that type of itching which has its origin in the skin. Fear, without " fight or flight " may bring on a severe attack of itching in Besnier's prurigo. One of us has seen an adolescent patient with this disorder in whom, when it was decided to carry out skin tests, the sight of the needle caused violent rubbing and scratching of the eyelids, forearms and legs to such a degree that within a few seconds the lids were exuding and the forearms and legs bleeding. Adrenaline is known to release histamine, the amount of which in the plasma rises steeply after an intravenous injection of 0·2 mg. of this drug (Staub, 1946).

The Central Nervous System.

We will now consider some evidence indicative of an abnormality in the central nervous system in Besnier's prurigo. O'Donovan (1952) had the concept that Besnier's prurigo might be a form of sensory fit analogous to idiopathic epilepsy. The orgies of rubbing and scratching which can be observed in these patients are often brief and separated by several hours in which there is little or no interference with the skin. O'Donovan had an electroencephalogram performed on one of his patients with Besnier's prurigo and it was found to be abnormal. We have therefore thought it worth while

to carry out a series of such examinations, using patients with various itchy dermatoses to form a control group. Volunteers upon whom itch powder had been dusted or a group of healthy young adults with scabies would have formed the ideal control group, by supplying an itchy dermatosis of established material causation, but we have had to be satisfied with the study of patients suffering from lichen simplex, prurigo ferox, dermatitis herpetiformis, or discoid eczema, conditions which some would call idiopathic and others would regard as partly or wholly activated by emotional stresses. The control group is not yet as large as we would like it to be, chiefly because of the difficulty of arranging electroencephalograms of patients in a severely itchy phase without undue interference with the more urgent work of the electroencephalographic department.

Before describing our findings it is well to mention the electroencephalographic investigations others have made on patients with dermatoses. It is only to be expected that patients with dermatoses associated with epilepsy should give abnormal electroencephalographic records. Thus, Dickerson and Hellman (1952) found a higher percentage of abnormal records in patients with tuberous sclerosis (epilepsy, adenoma sebaceum and mental deficiency) than in epileptics without this disease. Strauss, Ostow and Greenstein (1952) described three cases of this disease, all of which had an abnormal electroencephalogram. Watrin *et al.* (1951) also found abnormal tracings in this disease and in a case of von Recklinghausen's neurofibromatosis. Radermecker (1951) reports abnormal findings in encephalo-trigeminal angiomatosis, with epilepsy.

Chobot *et al.* (1950) studied 80 children between 4 and 14 years of age, with diagnoses of asthma, eczema, and allergic rhinitis, but without histories of convulsions, by electroencephalography, and found 33% abnormal. They found abnormal tracings in 16 of 52 asthmatics (31%), in 6 of 17 eczematous children (35%), and in 4 of 10 children with vasomotor rhinorrhoea (40%). Abnormalities were more common amongst females (13 of 32) than amongst males (13 of 48). Examination of parents and siblings (42 electroencephalograms in 22 families) revealed 16 with abnormal tracings (39%), 11 of whom were females.

Dees and Lowenbach (1948) found abnormalities in 50% of allergic children examined, but their cases included some with histories of convulsions. Huriez *et al.* (1953*a*) also found an abnormal tracing in a patient with ichthyosis. The skin condition was ameliorated by massive vitamin A therapy but the electroencephalogram was not modified.

Peterkin (1954) found an abnormal electroencephalogram in a patient with alopecia totalis; but the examination of 5 or 6 further patients with this disorder showed no abnormality. Huriez *et al.* (1953*b*) found abnormal electroencephalograms in two patients with congenital diffuse alopecia.

Michelson (1954) performed electroencephalographic examinations of 7 patients with lupus erythematosus who showed either psychic or neurologic findings, including one female during a phase of subacute systemic activity and at the height of a violent psychotic episode which followed steroid therapy. All the electroencephalograms were normal.

When our cases were examined with the electroencephalograph, we found a number of abnormalities of various kinds. These consisted of the occurrence of slow rhythms, of complexes containing fast and slow components and of sharp waves; the latter often occurred in groups. The slow waves could also sometimes be seen in the form of short-lasting high voltage runs. Although this type of record is not specific, the paroxysms of high voltage slow waves or of sharp waves, have commonly been seen in cases of epilepsy.

In Table II, the cases are divided into those under and those over 18 years of age. In the older group, the abnormalities seem to occur in a

TABLE II.

	Age over 18 years.		Age under 18 years.		Total.	
		%.		%.		%.
Normal	15	44	13	57	28	49
Doubtful	3	9	3	13	6	11
Abnormal	16	47	7	30	23	40
Total	34		23		57	

The proportion of abnormal electroencephalograms in the over 18 years age group (16 of 34) is significantly greater than the highest figure (15%) attributed to the general population ($S\chi^2 = 24{\cdot}962$: d.f. $= 1$: $P < {\cdot}001$).

The proportion for the under 18 years age group (7 of 23) is of doubtful significance ($S\chi^2 = 3{\cdot}173$: d.f. $= 1$: $0{\cdot}1 > P > 0{\cdot}05$).

higher proportion of cases. This appearance is due to the fact that slow rhythms, irregularities and occasional sharp waves occur in some electroencephalograms of children and adolescents. In young people we can only class an electroencephalogram as abnormal if these features are very pronounced. It can, therefore, be assumed that the 30% of abnormal records in patients under 18 years of age is really a minimum, rather than the true figure. In adults 47% showed abnormal electroencephalograms and in our total group 40%. This contrasts with 10–15% in the normal population. The sex incidence of the abnormal tracings was 12 of 36 males (33·3%) and 11 of 21 females (52·0%): 10 of 24 males over 18 years of age showed abnormal tracings but only 2 of 12 males under 18 years of age. Six of ten females over 18 years of age showed abnormal tracings and 5 of 11 females under 18 years of age.

Twenty-six other cases of itching dermatoses were examined. Of these 13 (50%) were normal, 6 (23%) were doubtful, and only 7 (27%) were abnormal. Abnormal electroencephalograms were obtained in discoid eczema (5 of 17 examined—29%), neurotic excoriations (1 of 2 examined) and lichen simplex (1 of 3 examined). This group is small and it is doubtful whether the findings can be regarded as significant. It certainly seems to contain a much smaller proportion of abnormals than does the group of Besnier's prurigo.

Comments.

Is there clinical evidence of a relationship between Besnier's prurigo and epilepsy ? In a recent survey of 52 cases of Besnier's prurigo, using a similar number of cases of acne vulgaris as a control group, we found a family history of epilepsy in 4 of the former and in 2 of the latter. No patient with prurigo or acne had personally suffered from epilepsy and a clinical association between the two diseases seems to be uncommon.

One of us has, however, seen two such patients since this survey was carried out. The first was a man, aged 43, who had suffered from severe nocturnal itching since the age of 30, shortly before his marriage. There was xeroderma, and pigmentation and lichenification of the antecubital fossae, fronts of the wrists and the backs of the forearms. There was no history of asthma or of hay fever, but for 3 years he had had attacks of epilepsy with tongue-biting and incontinence of urine. The electroencephalogram was described as diagnostic of epilepsy, with evidence of an epileptogenic focus on the right side.

The second was a girl, aged $4\frac{1}{2}$, who developed *petit mal* at the age of 4 and flexural prurigo at the elbows and knees 4 months later. The electroencephalogram showed a spike and wave activity.

Summary.

The most significant feature of Besnier's prurigo is an abnormality of immunologico-autonomic mechanisms.

The incidence of abnormal electroencephalographic tracings is significantly higher in Besnier's prurigo than in the general population.

Adrenaline, liberated by emotional and other stimuli but not dispersed in action in the vagotonic individual, may be responsible for the periodic liberation of histamine and general pruritus.

Itching may be widespread, and the localization of the dermatosis to the face, neck, flexures, wrists and elsewhere is determined, in part, by the easier accessibility of these areas ; in part by the higher content of histamine in the skin of the face and neck ; in part, once the lesions have become established, by the greater influence of circulating histamine on areas of skin partially depleted of histamine than on areas not so depleted.

In white dermographism the cells of the skin at the affected sites appear to have become refractory with the result that they do not release histamine in response to frictional stimuli.

In this skin disease, which is often accompanied by ichthyosis and sometimes by cataracts and in which abnormal electroencephalographic tracings are often found, it is probable that the fundamental pathological process pervades the whole epiblast (ectoderm).

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THE STATE OF THE BLOOD VESSELS OF THE FACE IN ROSACEA—II.

PETER BORRIE, M.A., M.D., M.R.C.P.
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THE fundamental feature of cutaneous rosacea is a persistent erythema in the central areas of the face. The pathogenesis of this erythema is unknown. One possibility is that the cutaneous blood vessels in this area are responding abnormally to one or more of the humoral controls which play a part in the maintenance of their tone. The following experiments were undertaken to investigate this concept.

MATERIAL.

Seventeen patients suffering from rosacea and seventeen normal subjects were investigated. The cutaneous blood vessels in the central area of the face were exposed to the action of adrenaline, *nor*-adrenaline, histamine and acetylcholine, introduced locally, and carbaminoyl choline, given systemically.

EXPERIMENTAL.

Adrenaline.—A solution of adrenaline, freshly prepared each day, was pricked into the prominence of the cheek, using a triangular cutting needle, care being taken not to draw blood. The concentration used varied from 1 : 1000 to 1 : 1,000,000 and the minimum concentration necessary to produce pallor was noted. This was found to be 1 : 10,000 in all subjects. When adrenaline was introduced by iontophoresis, using a copper electrode 1 cm. in diameter, a filter-paper 1 cm. in diameter dipped in the test solution, and a current of 1 ma. for one minute, the minimum concentration was found to vary between 1 : 1,000,000 and 1 : 100,000, equally in the two groups tested.

Finally, the negative pressure necessary to abolish the pallor produced by pricking in 1 : 1000 adrenaline was assessed. This was done by covering the area of pallor with a perspex cup half an inch in diameter, to which was attached by pressure tubing, a screw suction-pump, the negative pressure being measured by a mercury manometer included in the circuit. The average negative pressure necessary to abolish pallor on the cheek was 7 mm. Hg in the control group and 6 mm. Hg in the rosacea patients ; at a point half an inch in front of the pinna (an area usually unaffected in rosacea) the respective negative pressures were 33 and 30 mm. Hg.

Nor-*Adrenaline.*—The minimum concentration of this substance necessary to produce pallor when pricked into the cheek was found to be 1 : 1000 in all tested subjects. When introduced by iontophoresis the necessary concentration varied equally in the two groups between 1 : 100,000 and 1 : 10,000.

Histamine.—Histamine acid phosphate 1 : 3000 w/v was pricked into the

cheek, the flare and wheal being measured along two diameters at right angles to each other five minutes later. However, the response was vague, for the wheal was flat and definable by palpation only, and the flare faded imperceptibly into the normal erythema of the cheek. Exact measurements were, therefore, impossible but subjective assessment revealed no difference between the two groups tested.

The experiment was repeated by injecting 0·01 c.c. of a 1 : 10,000 solution intradermally. The subsequent wheals averaged 7·7 mm. in the rosacea patients and 7·6 mm. in the controls, while in both groups the flares averaged 30 × 20 mm. in diameter. The temperature of the skin 1 cm. from the site of injection was measured with a copper-constantan thermocouple before and five minutes after the injection; the rise was found to average 2·2° C. in the rosacea patients and 2·1° C. in the controls.

Histamine was also introduced by iontophoresis, in the same manner as that used for adrenaline, the concentration being 1 : 100,000, 2 ma. being passed for two minutes. The site tested was the centre of the forehead. In both groups the wheal averaged 12 × 10 mm. in diameter and the flare 25 × 25 mm. five minutes later.

Acetylcholine.—0·01 c.c. of acetylcholine was injected intradermally into the prominence of the cheek. Two concentrations were used—1 : 10,000 and 1 : 1,000,000—and the resulting erythema was measured five minutes later. No wheals resulted. The erythema caused by the higher concentration measured 20 × 14 mm. in the rosacea group and 20 × 16 mm. in the controls; and that by the lower concentration 21 × 15 mm. and 19 × 15 mm. respectively. Fifteen minutes after injection, the erythema had disappeared in 13 of the rosacea group and 14 controls. In those cases where it was still discernible it was faint and too ill-defined to be measurable, but subjective assessment revealed no difference between the two groups.

Carbaminoyl choline.—Carbachol was employed to investigate the systemic effect of choline esters, 0·25 mg. being injected subcutaneously into the arm. In neither group of subjects was there any increase of facial erythema in the subsequent half-an-hour.

Discussion.

Wetzel and Zotterman (1926) have shown that the depth of colour of the skin depends on the size of the capillaries and superficial venules. The deeper skin colours, such as that of the cheeks, occur where these vessels are dilated and this lack of tone is associated with a relative insensitivity to adrenaline. A further reduction in adrenaline sensitivity of the central facial capillary system could cause a persistent erythema, such as is found in rosacea. However, no such abnormal response was found, either to adrenaline or to *nor*-adrenaline.

The present investigation failed to demonstrate any abnormal reaction to histamine on the part of the facial skin blood vessels. That the erythema of rosacea could be caused by the action of histamine on blood vessels which react normally to this substance, is unlikely for the following reasons. Firstly, an accompanying oedema would be expected and this is not seen in rosacea. Secondly, antihistamine drugs would be expected to suppress, or at least to modify the condition and this does not occur. It was, therefore, considered unnecessary to investigate the effect of histamine-liberators in rosacea once it had been shown that there was no abnormal response to histamine in this condition.

One of the physiological effects of acetylcholine is to cause flushing of the face ; an abnormal response to choline esters is the basic feature in cholinergic urticaria (Grant, Pearson and Comeau, 1936) and Nomland (1944) has shown that this abnormality can result in an erythema, without accompanying oedema. No evidence was found in the present investigation, however, of any such abnormality in rosacea, whether the ester was given locally or systemically.

A number of other dilator substances have been discovered, occurring as natural constituents of animal tissues, such as adenosine and its derivatives (Bennet and Drury, 1931), substance P (Euler and Gaddum, 1931), bradykinen (Rocha e Silva *et al.*, 1949) and kallikrein (Kraut *et al.*, 1933). However, as yet, the evidence is quite insufficient for attributing to any of these substances a part in the control of human blood vessels, either in health or disease. It was, therefore, not considered reasonable to investigate their effects on the blood vessels in rosacea.

The results of these investigations suggest that the erythema of rosacea is not due to an abnormal response to any of the physiological substances which normally play a part in the maintenance of blood-vessel tone.

Summary.

The effect on the blood vessels of the central areas of the face of adrenaline, *nor*-adrenaline, histamine and acetylcholine, introduced locally, and carbaminoyl choline, injected systemically, was investigated in 17 rosacea patients and 17 normal controls.

No significant difference was found in the effects produced in the two groups of subjects.

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THE OXFORD DERMATOLOGICAL GROUP.

Reading, 4 September 1954.

Keratosis pilaris and Pseudopelade (consecutive macular atrophy)—Dr. H. T. Calvert.

A girl aged 7.

Family history.—Father, mother and older brother, aged 9, all have normal skins ; no known skin anomalies in her forebears.

Present illness.—Her mother states that she was born with a fuzz which fell, and that the hair never grew again properly over the vertex. However, the present trouble may be said to have started at the age of 2 with redness and scaling of the top of the scalp. Progression has been slow.

Examination.—Face : There is a faint erythema of the eyebrow area which varies in degree. The eyebrows are fine and scanty, especially to the outer sides, and the follicular openings are marked by pinhead conical papules some of which are devoid of hair and contain a fine horny projection. These conical papules are present also on the moustache area of the upper lip ; here they are not red but flesh-coloured. The cheeks are normal.

Scalp : The hair of the occiput is normal ; that of the temporal regions but little affected, an occasional hair showing a peri-follicular erythema or scale. The greatest change is seen towards the vertex : first a diffuse loss of hair, then little areas of scarred baldness the size of a split pea and finally the main area of irregular scarring, with scattered normal hairs singly or in groups. Marked inflammation can be seen about single or groups of hairs, leading in places to pustulation (*Staph. aureus* grown). This pustulation has been present only for the last six months ; before that there was only marked erythema and scaling. The normal hair present is rather coarse and curly.

Body : Scattered irregularly over back and chest, abdomen, upper arms and thighs is keratosis pilaris.

Investigations.—Repeated direct examination and culture for fungus proved negative.

Treatment.—Aureomycin by mouth followed by vitamin A, 50,000 units daily, and a salicylic acid ointment locally.

Progress.—Pustulation ceased and a little fine downy regrowth of hair of eyebrows and scalp commenced.

Comment.—This disorder was first described by Brocq, who stated that without keratosis elsewhere it would be impossible to separate it from pseudopelade.

Thirty-one other cases were shown by Dr. Calvert.

OBITUARY.

HOWARD FOX.

Dr. Howard Fox was born on 4 July 1873 in London, England, where his parents were living temporarily. After graduation from Yale University in 1894 and from the College of Physicians and Surgeons, Columbia University, in 1898, he interned for two years and then went to Europe. He studied dermatology in Berlin and in Vienna under the leading men of that era.

Upon his return to New York, he entered the service of his illustrious father, George Henry Fox, at the Vanderbilt Clinic and the New York Skin and Cancer Hospital. In 1908 Howard was elected a member of the American Dermatological Association and later served twice as president of the society. He was also one of the early members of the Manhattan Dermatologic Society, of which he later became president and honorary member. He was first president of the American Academy of Dermatology and Syphilology and for many years a member of the American Board of Dermatology, becoming president in 1945.

In 1936 Fox was elected to the Editorial Board of the *Archives of Dermatology and Syphilology* and one year later became Editor-in-Chief, a position which he held with outstanding ability for ten years. In his long and productive academic career he was first professor of dermatology at Dartmouth Medical School, then professor of dermatology and syphilology at the New York Polyclinic Medical School and subsequently was offered the chair of dermatology and syphilology at the School of Medicine, New York University. He held this for thirteen years. This appointment included a large ward and out-patient service at Bellevue Hospital.

Howard Fox was not only an eminent dermatologist, teacher, editor and leader in medicine. In addition, he had a splendid military record, starting in 1911 and continuing through two world wars, being commissioned a colonel of the Medical Reserve, United States Army, and appointed a consultant in tropical medicine to the Secretary of War.

At the time of his death on 19 October 1954, at the age of 81, Howard Fox was the revered and beloved Dean of Dermatology in the United States. He was an Honorary Foreign Member of The British Association of Dermatology.

CAT.

BOOK REVIEW.

Grenz Ray Therapy.*

We welcome this authoritative manual on a very valuable method of treatment. Bucky has been the pioneer and patient champion of the use of very soft x-rays, which has at last achieved wide acceptance.

In addition to the chapters by the two chief authors, there are contributions on Physics and Technique by O. Glasser and R. Steinitz, and Histologic Changes by M. A. Goldzieher: F. Sagher discusses the use of Grenz rays in Tropical Diseases, R. H. Brodsky in Oral Lesions, and F. Sagher and J. Landau in Ophthalmology.

The authors confine themselves strictly to the Grenz-ray range, i.e. HVL 0·015 to 0·035 mm. Al.; wavelengths 1 to 3 Å; kilovoltages 6 to 15.

The chapter on Histology is woefully inadequate. The observations are confined to experiments on the rat already published in Bucky's earlier book (1929), and a biopsy from one old man who had been irradiated 25 years previously, neither the dose nor the kilovoltage being known. No papers later than 1929 are mentioned.

Chapter 9, by Combes, is the most substantial and useful, consisting chiefly of a long list of individual disorders with notes on appropriate dosage. Their classification is odd: warts appear among inflammations, and rosacea among metabolic dermatoses. The order of the individual items follows no recognizable plan. A good many are included that are said to be unsuitable for Grenz rays. Among these it seems unnecessary to mention lipoma, which, together with a number of other unresponsive conditions, appears under the heading of Senile Keratoses. Psoriasis is given as a good indication, without any qualification; no reference is made to the unfavourable experiences of other authorities, e.g. Jungmann and Lomholt. Benign pigmented naevi are said to respond to Grenz rays, moderate doses being given every five weeks or so for periods up to more than a year. Bucky enjoins: "protection, repetition and perseverance." This seems a very risky procedure, and even then any hairs are left intact.

The section on vascular naevi is bewildering. Grenz rays are recommended for almost all varieties, especially the cavernous haemangioma, and one is depicted which appears to be at least the size of a greengage, which completely resolved after 23 treatments of only 275 r, HVL 0·028 mm. Al. One suspects that the involution was mainly, if not entirely, spontaneous. To explain the surprising responsiveness, he points out that the cells composing a cavernous haemangioma are immature. "To be affected by ionizing radiation, the vital cell must be capable of absorbing some fraction of the radiant energy." Even air and water are capable of absorbing some fraction of the radiant energy, and the authors have been at pains to iterate how much of the incident dose is absorbed by the "dead" horny layer. "Many patients have received in one area as much as 20,000 r over a ten year period." Yet, "If no response is observed in adults after a total dosage of 5000 r, there is no reason to continue therapy."

There are some very loose statements, e.g. that lupus vulgaris and malignancies "require special discussion, in so far as these diseases usually affect the regenerative and nutritive strata of the skin": and platitudes are reiterated: "Radiation with

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* *Grenz Ray Therapy.* By G. Bucky and F. C. Combes. (1954) New York: Springer Publishing Co. and distributed by Lange, Maxwell & Springer Ltd., London. Pp. 204. 62 figs. Price: £3.

little penetrating ability cannot reach deeper tissues because it is absorbed by the upper layers."

Verbal infelicities are common, e.g. "penetrability" of Grenz rays. A negative seems to have been omitted in the following sentence: "Although the output of the tube is roughly proportional to the current, it is advisable to use this relationship for the calculation of dosages" (page 26). Hidradenitis is throughout mis-spelt "hydradenitis."

There is a useful classified bibliography, in addition to the lists of references at the end of each chapter.

In spite of numerous imperfections, dermatological radiotherapists will rightly want to have this book at hand, and will find it helpful.

W. N. G.

Porphyrins.*

In this comprehensive monograph on porphyrins, Prof. Vannotti, a well known worker in the field, presents his own conceptions and interpretations of the biological and clinical importance of these widespread pigments, and because some of his views are not coincident with the views of others, his presentation is the more valuable. The excellent translation into English is by Prof. C. Rimington, who has also made amendments and additions to the chemical sections necessitated by recently published work (the preface is dated 1952).

A well-documented account of the occurrence of porphyrins at all levels of the animal and plant worlds (haems and haemoglobins, cytochromes, chlorophyll, etc.), details of their extraction, and their chemical and physical properties occupies a quarter of the book. As befits a monograph published under the auspices of Hilger & Watts, the optical instrument manufacturers, tables and photographs of absorption- and fluorescent-spectra abound.

Then Vannotti considers the pathways and products of human porphyrin formation and metabolism in normal and pathological states. The pathological metabolism of porphyrins is especially evident in functional disorders and lesions of those organs intimately concerned with the metabolism of these pigments, chiefly the digestive tract, the liver, the bone-marrow and the skin, and is also evident in general pathological conditions such as intoxications and hypovitaminoses. Not only the clinical findings are given, but also Vannotti's interpretation of the biological changes involved, for example, the mechanism of photosensitisation by porphyrins. Separate and lengthy consideration is given to the true porphyrias, in which the exaggerated production of porphyrins is the primary manifestation, causing a series of related secondary clinical symptoms to appear. Cutaneous lesions, pigmentation and photosensitivity consequent on porphyria are adequately discussed, with case-histories and photographs, and a chapter (possibly over-encouraging) on treatment.

J. B. J.

Leg Ulcers.†

In this interesting monograph, the present state of knowledge concerning leg ulceration is ably presented. The scholarly erudition of Dr. Anning's approach is admirable, and combines with an exceptional bibliography to form a treatise which may almost be described as enjoyable, if such an adjective is permissible in association

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* *Porphyrins—Their Biological and Chemical Importance.* By A. Vannotti. Translated by C. Rimington. (1954). London: Hilger & Watts Ltd. Pp. 258. 15 Plates. Price 50*s*.

† *Leg Ulcers: Their Causes and Treatment.* By S. T. Anning, T.D., M.A., M.D., M.R.C.P. London: J. & A. Churchill Ltd. Pp. 178. 42 Illus. Price 18*s*.

with the pedestrian subject. He has, in addition, performed a valuable service in emphasizing the general medical aspects of individual patients with leg ulcer which will be of help to the junior surgeon who has, not infrequently, many such cases under his charge.

Were any criticism to be made, it would be that since the practical aspects of this condition tend to outweigh the theoretical considerations, the portion of the text devoted to treatment (one-fifth of the whole) is disappointingly short. Inclusion of the results of treatment and the analyses of any cases of recurrence might even further improve this excellent book. J. F.

CORRESPONDENCE.

To the Editor of The British Journal of 'Dermatology.'

Sir,—With reference to my case report " Congenital poikiloderma with traumatic bulla formation and progressive cutaneous atrophy " (*Brit. J. Derm.*, 1954, **66**, 104) I should like to draw attention to two cases published earlier by A. Sorsby, J. A. Fraser Roberts and R. T. Brain (*Doc. opth.*, 1951, **5–6**, 118), which I think have a great resemblance to the one I reported. Although I saw those patients a few years ago, the association with my case did not occur to me until I lately re-read the paper.

Two sisters, aged 56 and 51 years, had been suffering from a generalized skin condition from the age of 18 months and six years respectively. There had been blister formation on skin and mucous membranes which had become less frequent in recent years. Both sisters had a generalized severe atrophy of the skin with areas the appearance of which suggested poikiloderma. The hands were deformed, the skin of hands and feet was tense, thin and glossy. There was dystrophy of the nails and symmetrical fusion of the proximal parts of fingers and toes. The mucous membrane of the mouth was atrophic. There was also essential shrinking of the conjunctiva and in one sister vesicle formation on the cornea.

Except for the eye symptoms, all the features occurring in these two patients were also present in my case. The histology likewise was similar in that it showed atrophy of the epidermis, sub-epithelial cleft formation, disappearance of the elastic tissue in the upper cutis, degenerative changes of the collagen, and increase of capillaries in the cutis.

The mode of inheritance was of the recessive type, as in the majority of cases of dystrophic epidermolysis bullosa and as is equally frequent in congenital poikiloderma and the probably allied condition of Rothmund s syndrome.

In discussing the diagnosis the authors suggest that their cases have many features of recessive epidermolysis bullosa ; they also state that the skin lesions are in many areas suggestive of poikiloderma.

Allowing for the difference in ages which would account for the fact that the skin condition has in the two sisters reached a terminal stage of atrophy while it is still in an earlier period of development in my 14-year-old patient. I think that there is a great similarity in the cases. Besides wanting to make amends for my omission to mention the earlier publication, I also wish to draw attention to another instance of this hitherto not reported association of epidermolysis bullosa dystrophica, congenital poikiloderma and idiopathic atrophy of the skin.

I am, Sir,

Yours, etc.,

THERESA KINDLER.

London, W.1.

November, 1954.

CURRENT LITERATURE.

STUDIES WITH THE TREPONEMAL IMMOBILIZING TEST. J. L. Miller, M. H. Slatkin, M. Brodey, H. L. Wechsler and J. H. Hill. (1954) *J. Amer. med. Ass.*, **154**, 1241.

This article contains so much important information that it should be read in the original. The specificity of the treponemal immobilizing test (T.P.I.) is confirmed. Unless adequate treatment has been given at an early stage the T.P.I. appears to remain positive indefinitely in all cases of syphilis. It is also positive in yaws, bejel and pinta. It cannot be used as a guide to treatment.

The T.P.I. provides no evidence that any one of the various serological tests in use is more reliable than any other in the diagnosis of syphilis. Too much significance has been attached to the titre of serological tests. Some patients with high titres have been shown to be false positive reactors.

While biological false positive reactions to serological tests occur in acute disseminated lupus erythematosus, such reactions are so uncommon in sarcoidosis that a positive serological test in this condition should be regarded as evidence of syphilitic infection. Fourteen of 102 patients with sarcoidosis had positive serological tests for syphilis. The T.P.I. was carried out in 11 of these and was positive in 10.

In many other diseases in which biological false positive reactions are known to occur the T.P.I. is of great value. Numerous instances of misinterpretation of serological reactions in both directions have been encountered. Evidence is presented that the antibody responsible for the T.P.I. passes the placental barrier. A. J. R.

CAT SCRATCH DISEASE. W. B. Daniels and F. G. MacMurray. (1954) *J. Amer. med. Ass.*, **154**, 1247.

Cat scratch disease was apparently first recognized by Foshay of Cincinnati in 1932. In the last ten years many cases have been reported from Europe and from the United States, and the clinical and pathological features are now well defined. Skin testing with the specific antigen provides useful confirmatory evidence when the diagnosis is suspected. This article is based on the analysis of 160 cases. Over one-third of the patients were under 10 years of age. There were 12 household epidemics centring round the family cat. Ninety-eight patients had been scratched or bitten by cats and only 12 gave no history of contact with cats. The clinical manifestations simulate a wide variety of other conditions, including primary tuberculosis, infectious mononucleosis, pyogenic infections and tularemia. The oculo-glandular form (Parinaud's Syndrome) is characterized by intense unilateral conjunctivitis with enlargement of the preauricular lymph node, fever and malaise. An evanescent rash occurred in 11 cases, and erythema nodosum in 2. Two cases complicated by encephalitis have been reported. The aetiological agent has not been identified. A. J. R.

DELUSION OF PARASITOSIS. I. Aleshire. (1954) *J. Amer. med. Ass.*, **155**, 15.

Patients with delusions of parasitosis seldom respond to psychiatric or other treatment. A patient with pellagrous psychosis, dermatitis, neurotic excoriations and trichotillomania recovered completely on an antipellagrous régime. Three other patients with delusions of parasitosis, but no clinical evidence of pellagra were found to have taken an inadequate diet for long periods and were therefore treated on the same régime. All were cured of their delusions. A. J. R.

HORMONE CREAMS AND THE FACIAL SKIN. H. T. Behrman. (1954) *J. Amer. med. Ass.*, **155**, 119.

The local application of oestrogens to senile skin can produce slight epidermal hyperplasia, detectable histologically. As the result of this observation certain "hormone creams" have been put on the market by American cosmetic manufacturers. Three such creams containing from 7,500–15,000 international units of oestrogen in each ounce were submitted to carefully controlled clinical trial. No visually appreciable difference was observed between the side of the face treated with the cream and that treated with the base alone. A. J. R.

INDOLENT FOLLICULAR SUPPURATION UNDER "MELANIC" NAEVI. B. Duperrat. (1954) *Ann. Derm. Syph., Paris*, **81**, 251.

Eleven patients are described in whom increase of size in melanic naevi was due to chronic underlying follicular infection and not, as might have been suspected, to malignant change. F. F. H.

EXPERIENCE IN THE TREATMENT OF PELLAGRA WITH ACTH. D. K. Miowski and I. S. Tadzer. (1954) *Ann. Derm. Syph., Paris*, **81**, 259.

The authors quote evidence showing that there is a dysfunction of the suprarenals in pellagra. They treated 5 pellagrins with ACTH with very satisfactory results. F. F. H.

Arch. argent. Dermatologia. (1953) **3**, No. 3.

All the contributions by various authors to this number are on affections of the lower limbs, conditions that form about 30% of the cases attending dermatological clinics in Argentina. The introductory paper on the anatomy and physiopathology of the venous system of the legs is supported by phlebographic studies which have confirmed the view that in the horizontal position there is no communicating flow of blood between the superficial and the deep veins. In the erect position the pressure in normal superficial veins is equal to the orthostatic pressure in varicose veins and the valves open when the pressure below becomes greater. Muscular contraction empties deep veins and relaxation aspirates blood through the communicating veins from the superficial to the deep system. When the valves are incompetent the veins feel the effects of orthostatic pressure all the time. Anoxia of the tissues follows and the disturbed metabolism of the capillaries and endothelial lining of the veins gives rise to trouble. Ferreira has never found a chronic ulcer develop on a leg when only the superficial system of veins was at fault.

Pierini writes on bacterial dermoepidermitis and on the pigmented purpuric dermatoses which he groups under the heading of angiodermites or cutaneous haemosiderosis. Although angioma serpiginosum does not show haemosiderin, it is included in the group. G. W. B.

THERAPY OF CHRONIC ULCERATION OF THE LEGS ASSOCIATED WITH SICKLE CELL ANEMIA. A. I. Chernoff, J. B. Shapleigh and C. V. Moore. (1954) *J. Amer. med. Ass.* **155**, 1487.

From 30%–50% of all persons with sickle cell anaemia suffer from leg ulcers at some time during their lives. The ulcers are often painful and difficult to heal. In six patients the ulcers healed rapidly with bed rest when the haemoglobin level was maintained near normal by transfusions. A. J. R.

NITROFURAZONE DERMATITIS FOLLOWING COITUS. C. George. (1954) *J. Amer. med. Ass.*, **156**, 247.

The husband of a woman who was using nitrofurazone suppositories developed itching and burning of the penis a few hours after intercourse. Intercourse took place on the two following days and the patient developed a dermatitis of penis, scrotum, thighs and wrists. A patch test with nitrofurazone was positive. A. J. R.

PITUITARY BASOPHILISM IN THE JUVENILE TYPE OF ACANTHOSIS NIGRICANS. S. Rothman. (1954) *J. Amer. med. Ass.*, **156**, 242.

An interesting report of a case of acanthosis nigricans of benign juvenile type in which diffuse basophilism of the pituitary gland was discovered at autopsy. Possibly basophilism will be found in other cases of this form of acanthosis nigricans as it is perhaps capable of giving rise either to this syndrome or to Cushing's syndrome, two conditions clinically distinguishable but with much in common. A. J. R.

KERATOACANTHOMA. E. J. Levy, M. M. Cahn, B. Shaffer and H. Beerman. (1954) *J. Amer. med. Ass.*, **155**, 562.

A good account of the clinical and histological features of keratoacanthoma. The first cases to be reported in the United States are described with informative illustrations. The authors suggest that if the diagnosis is in doubt the lesion should be treated as an epithelioma. A. J. R.